

weight with about 0.1% to about 4% w/w of one or more pharmaceutically acceptable rate controlling polymers.

**Remarks**

Reconsideration of the above-identified patent application, as amended, is respectfully requested.

Upon entry of this Amendment, Claims 1, 2 and 5-12 will be pending in the Application.

The present amendment finds support in all the examples of the application as filed, and in the Summary as filed, for example, see page 9, lines 5-6. The total weight of the tablet does not exceed more than 1500 mg containing the maximum amount of drug, i.e., 1000 mg in the composition, which is about 66% w/w of the total tablet weight.

In the Office Action dated February 21, 2002, the Examiner rejected claim 11 under 35 U.S.C. 102(b) as being anticipated by USP 6,010,718 (Al-Razzak et al.). The Examiner further rejected claim 11 under 35 U.S.C. 103(a) as being unpatentable over Al-Razzak et al. The Examiner also rejected claims 1-10 and 12 under 35 U.S.C. 103(a) as being unpatentable over Balkin (USP 5,656,284) in view of Urquhart et al. (USP 4,851,232).

Applicants believe that claim 11 as amended herein is not anticipated by Al-Razzak et al. The objective of the present invention was to develop a controlled release formulation for once daily administration of erythromycin or derivatives thereof, that carries a large payload of the drug and which is of an acceptable size and further, which is convenient for oral administration. The instant invention achieves this objective by using small amounts of rate controlling polymers. Al-Razzak et al., on the other hand,

discloses a dosage of 500 mg of clarithromycin in a 900 mg tablet (Example 1). A single table containing 1000 mg clarithromycin, for once daily administration, according to Al-Razzak et al. would be unacceptably large at 1800 mg for human consumption.

Rejection of claims 1-12 Under § 103(a)

Applicants believe that claims 1, 2 and 5-12 as presented herein are unobvious over Balkin in view of Urquhart et al. As is well known, to establish a prima facie case of obviousness, three criteria must be met. First, there must be motivation in the prior art references to modify the reference. Second, there must be a reasonable expectation of success and third, the prior art reference must teach or suggest all the claimed limitations. In this connection, all the teachings and suggestions as well as the expectation of success must come from the prior art and not from the Applicants' disclosure.

The formulation of the present invention was specifically developed for once daily administration of the adult dose of 1000 mg of erythromycin or derivatives thereof thus obviating the need for administration of two tablets of 500 mg.

Reviewing the two references Balkin or Urquhart et al., there is no suggestion of the desirability of developing a formulation suitable for once daily administration. Balkin discloses a transmucosal tablet to be held in the mouth between the mucosa of the lip and the opposed gingival mucosa. The amount of drug used and the mechanism of drug release from transmucosal tablets is entirely different from that of controlled release tablets. While transmucosal tablets are suitable only for low dose drugs whereas, the controlled release tablets such as described in the instant invention carry a very high payload of the drug.

Admittedly, the organic polymers used in accordance with Balkin include xanthan gum. However, in col. 3, lines 63-67, the inventors describe that the organic polymers

are chosen as they form strong gels which allow unhindered movement of the non-polymer (which is drug) molecules within them. In contrast, the oral controlled release formulation as described in the instant invention prevents immediate release of the drug and sustains the rate of drug release over an extended period of time even in the presence of large volumes of liquid present in the stomach and the gastrointestinal tract.

Urquhart et al. describes a drug delivery device for the controlled delivery wherein the drug pills are coated with a release rate controlling polymer and embedded in a reservoir of hydroxypropyl methyl cellulose or other similar polymers. Urquhart et al. describes a delivery system wherein large amounts of release rate controlling polymers are used in the reservoir surrounding the polymer coated pills (see Example 1). In contrast, the instant invention controls the drug release using very small amounts (0.1 – 4%) of release rate controlling polymers.

Further, it is clear that neither the problem nor its solution is discernible to one with ordinary skills in the art from the teachings of Balkin in view of Urquhart et al. It is, therefore, felt that the Examiner has failed to make out a *prima facie* case of obviousness and for this reason alone, the obviousness rejection should be overturned.

Applicants believe that claim 11 as presented herein is also unobvious over Al-Razzak et al. for the same reasons as discussed above. There is no motivation or teaching in Al-Razzak to modify the reference to develop a controlled release formulation using small amounts of rate controlling polymers so that it can carry a large payload of the drug thus resulting in smaller tablet which are suitable for oral administration to humans. There is also no reasonable expectation of success. The use of polymers for sustaining the rate of drug release is well known in the art but the novelty of the instant invention is that it is achieved suing small amounts of polymers, thus allowing-for-larger amount-of drug to be loaded into the dosage unit. It is, therefore, felt that a *prima facie* case of

obviousness has not bee made and for this reason alone, the obviousness rejection should be overturned.

Election Under § 121

Applicants believe that claims 1-12 as presented herein are in fact novel and patentable over cited references. However, if no generic claim is finally held to be allowable, applications would like to elect "cellulose ether" species to be prosecuted on the merits.

Conclusion

For the reasons stated above, the Examiner is urged to pass amended claims 1, 11, 12 and dependent claims 2, 5-10 to issue immediately. A clean copy of the claims as amended is submitted herewith, and authorization is hereby given to charge any fees deemed to be due in connection with this Amendment and Response to Office Action to Deposit Account No. 50-0912.

Respectfully submitted,

RAMPAL *et al.*

By:

  
\_\_\_\_\_  
Jayadeep R. Deshmukh, Esq.  
Reg. No. 34,507

Date: August 21, 2002

Ranbaxy Laboratories Limited  
600 College Road East, Suite 2100  
Princeton, New Jersey 08540  
Tel: (609) 720-5608  
Fax: (609) 514-9779